

REMARKS

Reconsideration of the application is respectfully requested in view of the following remarks.

I. STATUS OF THE CLAIMS

Claims 1-17, 17, 21, 22, 25-29, 31, 33, 34, 36-38, 41, 46, 52, 54, 55, 68, 70-76 and 79-85 are pending, with claims 17, 21, 22, 25-29, 31, 33, 34, 36-38, 41, 46, 48, 52, 54, 68, 70-76 and 80-85 being withdrawn for being directed to a non-elected invention.

Claims 1, 3, 11, 17, 82, 84 and 85 are amended herein and claims 2, 14, 48, 54, 55 and 80-83 are canceled. New claims 86-92 are added herein. Support for the amendments can be found throughout the application-as-filed. See, for example, original claims 2 and 14. Support for new claim 86 can be found, for example, at page 2, line 23, through page 3, line 3, of the application-as-filed. Accordingly, no new matter has been added. Moreover, all of the amendments overcome the rejections and/or adopt suggestions from the Examiner and/or eliminate issues for appeal, so entry of the amendment is respectfully requested.

Various full names have been included in claims that used acronyms, rendering moot the Examiner's objections to certain claims, without narrowing claim scope.

The amendments made herein are solely to expedite prosecution of the application and not for reasons pertaining to patentability. Applicants reserve the right to pursue the subject matter of any claim (whether original, amended or canceled) in continuing applications.

II. THE REJECTIONS BASED ON PRIOR ART SHOULD BE WITHDRAWN.

The Office maintained the rejection of various claims as allegedly being anticipated by, or rendered obvious by, Parr et al. (2003), alone or in combination with other references. The Examiner's basis for maintaining the rejection is because the declaration pursuant to 37 C.F.R. 1.131 submitted in response to the previous Office Action failed to state that the work was performed in the U.S., a NAFTA country or a WTO country.

In the telephonic interview with the undersigned and David A. Gass on September 10, 2010, the Examiner indicated that the declaration would be accepted if revised to state that the work was performed in one of the accepted territories. Submitted herewith is a revised

Rule 131 declaration establishing that the inventors invented the invention in Finland (a WTO country) before the publication date of Parr et al. (alleged to be publicly available as of July 17, 2003).

In addition, the Applicant's submission dated May 3, 2010 included an explanation from the inventors and confirmation from the undersigned attorney that the invention was communicated to U.S. Patent Counsel (in the United States) prior to the purported publication date of Parr et al. The communication of the invention to U.S. counsel also satisfies the requirements of antedating the reference.

Because the primary reference is not citable as statutory prior art, the rejections based on prior art are moot, and should be withdrawn.

III. THE REJECTION ALLEGING INDEFINITENESS SHOULD BE WITHDRAWN.

The Office alleged that claims 1-15 and 79 were unclear because there is no required method step wherein an 'elevated Prox-1 expression or activity' is in fact detected. The Applicants amend-in-part and traverse-in-part.

Claim 1 has been amended to explicitly recite a frame of reference of the claimed screening. In particular, the claim now specifies that elevated expression "compared to Prox-1 expression in healthy colon tissue" correlates with the presence of colon cancer. An analogous new claim 86 is added, reciting a comparison in relation to colon cancer tissue. It is believed that these amendments render moot the rejection, and it should be withdrawn. The added clauses explain the nexus between the measurement and the conclusion to be drawn in the screening step.

To the extent that the rejection is stating that the claims are indefinite if they do not require a positive result (elevated expression), the Applicants traverse. It is commonplace in the medical field to perform a diagnostic screening assay for disease states in which one or more parameters are measured, and a diagnosis – positive *or negative* – is reached depending on the measurements. A person of ordinary skill understands that when an abnormal measurement (in this case an elevated measurement), relative to a healthy control, correlates

with a disease, then a normal measurement (in this case, the absence of the elevated measurement) is not scored as a diseased subject. Some tests come back positive, and some tests come back negative. Both situations fall within the ambit of a medical screening assay. Wikipedia explains “Diagnostic test” to the layperson in just this way: “The result of a test may be **positive** or **negative**: this has nothing to do with a bad prognosis, but rather means that the test worked or not, and a certain parameter that was evaluated was present or not. For example, a negative screening test for breast cancer means that no sign of breast cancer could be found (which is in fact very positive for the patient).” (See http://en.wikipedia.org/wiki/Diagnostic_test) There is nothing unclear about how to perform the screening as currently claimed.

The Office asserts that a method wherein no Prox-1 elevation is detected “is not consonant with the ‘wherein’ clause, which...appears to require elevated expression.” The wherein clause requires elevated expression in order to diagnose the presence of colon cancer. The wherein clause does not, however, require the subject to have elevated expression. A subject without elevated expression is not diagnosed with colon cancer according to this screen.

In addition to the foregoing remarks, the Applicants have added new claims 79 and 92 which specify the elevate/positive response. Accordingly, the rejection is moot and should be withdrawn.

IV. THE REJECTION ALLEGING LACK OF ENABLEMENT SHOULD BE WITHDRAWN.

The Office alleged a variety of reasons why the Office believed the full scope of the claims was not enabled. The Applicants respectfully traverse.

The Office first alleged lack of enabling disclosure with respect to “methods as claimed which encompass any level of elevated expression or activity.” While Applicants continue to disagree with the Examiner, independent claim 1 as amended herein recites that an elevated level of Prox-1 expression detected in the colon tissue sample compared to the level of Prox-1 expression in healthy colon tissue correlates with the presence of colon cancer in colon tissue, which is fully enabled by the application-as-filed. See, for example, Example

2 which reports that both Prox-1 mRNA and protein expression is elevated in colon cancer tissue samples compared to healthy tissue samples. Reference to Prox-1 “activity” has been deleted, to expedite allowance.

The Office continued to allege lack of enablement with respect to “any pathological condition.” All of the pending claims are directed specifically to colon cancer, and not any pathological condition as alleged by the Examiner. Thus, this aspect of the rejection is improper.

The Office continued to allege that the specification does not provide any evidence directly establishing that elevated Prox-1 protein correlates with colon cancer, or establishing the same indirectly by showing that the elevated Prox-1 mRNA correlates with elevated Prox-1 protein. In fact, the application-as-filed demonstrates that increased Prox-1 protein expression (compared to adjacent normal mucosa) was identified in 9 of 11 human colorectal adenomas and also in 6 of 9 human colorectal carcinomas. See page 60, line 23 through page 61, line 3. Thus, the application clearly demonstrates that elevated Prox-1 protein expression is observed in colon cancer.

Further, subsequent to the filing date of the present application, additional experiments were performed to evaluate the immunohistochemical expression of Prox-1 protein in colon tissue from 517 colorectal cancer patients compared to the colon tissue of healthy subjects. A Rule 132 Declaration from Dr. Kari Alitalo, submitted herewith, describes the results of the additional experiments. Briefly, his research team observed elevated Prox-1 protein expression in 91% of the tumor samples tested (471/517), whereas the healthy tissue samples were negative for Prox-1 expression, with the exception of a few crypt and neuroendocrine cells. These data confirm the teachings of the application-as-filed that elevated Prox-1 expression is present in colorectal cancer tissue samples compared to healthy tissue samples.

Finally, the Office continued to assert that the results provided in the application could not be extrapolated to other mammals. While Applicants continue to disagree with the Examiner, and do not believe that the Office has carried its burden of supporting a rejection,

the claims have been amended to recite methods of screening, etc. in a human subject. Thus, this aspect of the rejection is moot.

In view of the foregoing, Applicants request that the enablement rejection be withdrawn.

V. CLAIMS 82 AND 84-85 SHOULD BE REJOINED AND ALLOWED.

The amendments to claims 82 and 84-85 make these claims more similar to the elected claims. Moreover, the Parr reference relied upon (in part) for the unity analysis has been effectively removed as a reference. Accordingly, the Applicants request that these claims be regrouped with the elected claims and examined on the merits.

VI. TREATMENT CLAIMS (CLAIMS 17, 46, AND OTHERS) SHOULD BE REJOINED AND ALLOWED

The Office's stated position – in the context of discussing the Parr reference – is that it would have been *prima facie* obvious to administer a Prox-1 inhibitor if taught by Parr that Prox-1 was over-expressed in colon cancer. Applicants reserve the right to dispute this position, though it is moot in view of the antedating of Parr. However, it is inconsistent for the Office to maintain its restriction requirement – dividing screening and treatment claims – while maintaining at the same time that the treatment would be *prima facie* obvious from the over-expression data that supports the screening.

VII. CONCLUSION

For the foregoing reasons, the application is believed to be in condition for allowance. If any fees necessary for entry of this response are unpaid, the Office is authorized to charge Deposit Account No. 13-2855 under Order No. 28113/39467A. The Examiner is invited to telephone the undersigned if a telephone conference would expedite prosecution.

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Respectfully submitted,

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